

## Carcinoma of Urinary Bladder in Young Patients

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### Abstract

**Introduction:** Urothelial carcinoma of urinary bladder is rare before age of 40 years. The issue regarding age is critical because the behavior of tumor at different age group is a matter of great debate. Our study aimed to see the grade and stage of disease at the time of presentation and its recurrence as well as progression after 3 month at first check cystoscopy in young patients.

**Method:** We prospectively analyzed our newly diagnosed twenty consecutive patients up to 40years of age (16 males – 04females) with urothelial carcinoma of urinary bladder, who were treated at our hospital. The data was reviewed regarding age of patients, stage and

PGMI / Lahore General Hospital, Lahore grade of tumor at time of presentation. The recurrence and progression after 3 months at first check cystoscopy was noted.

**Results:** Twenty consecutive patients of 21 to 40 years of age who were diagnosed as urothelial carcinoma of urinary bladder were analysed. The mean age at time of diagnosis was 32.2 years, male to female ratio was 4; 1. Painless hematuria was a predominant symptom in all cases, while 20% (n – 4) had irritative symptoms along with hematuria. The stage at first resection was as pTa (60%), pT<sub>1</sub> (20%), pT<sub>2a</sub> (10%) and pT<sub>2b</sub> (10%). The grade of disease at initial diagnosis was low grade in 90% of cases (well differentiated in 60% of cases, moderately differentiated in 30%) while 10% had high grade disease. At first check cystoscopy after 3 month only 2 patients had recurrence out of 16 patients who had superficial disease. The remaining four patients who had muscle invasive disease were advised radiotherapy / radical cystectomy. They opted radiotherapy. Among these four patients two came on follow up and their cystoscopy reveal a very small recurrence which was resected. The remaining two did not turn up for follow up. No progression was noted.

**Conclusion:** Biological behavior of urothelial bladder cancer depends upon stage and grade. The young patients have good prognosis as they are having low grade and stage.

### Introduction

Urothelial tumor of urinary bladder is one of the commonest malignancies of genitourinary tract. The me-

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dian age of presentation is 6<sup>th</sup> and 7<sup>th</sup> decade of life.<sup>1</sup> This is rare in first decade of life. Cases of bladder cancer have been reported in children and also during pregnancy.<sup>2,3</sup> Regarding incidence of disease in younger age (up to 40) reports are conflicting ranging for 0.8 % (4) to 3.6% (5). The age of 40 years is selected for the reason that disease is relatively uncommon and rises after 40 years.<sup>4</sup>

The biologic behavior of bladder tumor is under study worldwide and conflict exists about the recurrence and prognosis in less than 40 years age.<sup>6</sup> According to some investigator the behavior of disease depends upon grade and stage of disease, while others believe that younger patients have better prognosis as compared to old age group.

In our study we shall evaluate the age, symptoms, grade and stage of disease at time of presentation. The grade and stage will be assessed after first resection and histology of specimen. The size and multiplicity will also be noted. The recurrence and progression of disease was noted after 3 months at 1<sup>st</sup> check cystoscopy. The trend is changing particularly in low risk group regarding the follow up. If there is no recurrence at 3 months subsequent recurrence chance is less in low grade and low stage disease.<sup>7</sup>

## Aims and Objective

1. To find out grade and stage of disease in younger age group.
2. To assess the behavior of disease (recurrence, progression) at first check cystoscopy.

## Materials and Methods

This prospective study was carried out at department of urology Post Graduate Medical Institute / Lahore General Hospital Lahore between – 2008 to 2011. All the patients of both sexes up to 40 years of age with established transitional cell carcinoma of urinary bladder were included. Demographic data history, physical examination and required investigations carried out. Under general / spinal anesthesia bimanual examination done. The urethroscoposcopic findings like site, size, shape, and number of growths were noted before transurethral resection. Transurethral resection of bladder growth was performed. Histopathology findings were studied. Recurrence and progression was observed after 3 month at first check cystoscopy. The staging was done according to tumor node metastasis clas-

sification (TNM). The grade was assigned according to WHO criteria, grade 1 and 11 as low grade disease and grade 111 as high grade disease. Intravesical immuno-therapy Instilled in patients with pT<sub>1</sub> G<sub>11</sub>, having multi lesion disease, and with high grade disease cases weekly for six weeks. The disease progression was defined as conversion by pathological stage from superficial to invasive bladder cancer.

## Results

In our study mean age at time of diagnosis was 32 years ranging from 21 – 40 years. Among these 40% were between the age of 21 – 30 years and 60% had age from 31 – 40 years. The male to female ratio was 4: 1 (16 Male and 4 Female). In this study we followed the patients till first check cystoscopy at 3 months. Painless hematuria was present in all patients and 20% patients had the irritative symptoms associated with hematuria. Occupational details were as 40%<sup>8</sup> patients were farmer, 20%<sup>4</sup> were factory worker (boiler engineer and metal industry), 20% house workers, while 10% (2) office workers and shopkeeper each. Smoking was found in 6 (30%). The histopathological diagnosis after resection came out as 16 (80%) had superficial disease and 4 (20%) had muscle invasive disease. The stage of disease at the initial diagnosis was as follow pTa (n = 12), pT<sub>1</sub> (n = 4), pT<sub>2a</sub> (n = 2), pT<sub>2b</sub> (n = 2).

We divided these 20 patients into two groups. Group 1 was from age 21 – 30 years has 8 patients (40%) and in group II from 31 – 40 years has 12 patients (60%). All the patients in group I had superficial disease with low grade. Among 12 (60%) patients in group II, 8 had superficial disease and 4 had muscle invasive disease (pT<sub>2a</sub> and pT<sub>2b</sub>). In group II the 8 patients having superficial disease had low grade. The 4 patients in group II who were having muscle invasive disease 02 had low grade disease and other 2 had high grades.

Intravesical BCG was instilled in 4 patients and these included 01 patient in group one who had pT<sub>1</sub>, G<sub>2</sub>, 03 in group II who had pT<sub>1</sub>, G<sub>2</sub>. No recurrence was noted in group I but 02 patients in group II who had pT<sub>1</sub> G<sub>2</sub> and multiple lesions had recurrence. Among the remaining four patients who had muscle invasive disease with high grade 02 opted for radiotherapy and at 1<sup>st</sup> check cystoscopy developed small recurrence which was resected. No progression was noted

in any group who were followed. Two patients lost to follow up.

### Characteristics of Patients Treated For CA Bladder

Association of Age with the Stage of the Tumor

Stage of Tumor	Age Groups					
	21 – 30 Years		31 – 40 Years		Total	
	No.	%	No.	%	No.	%
Superficial (PTa, Pt <sub>1</sub> )	8	40.0	8	40	16	80.0
Muscle Invasive and Metastatic	0	0	4	20.0	4	20.0
Total	8	40.0	12	60.0	20	100.0

Statistical Analysis: P – value for Fisher exact = 0.116

Association of Age with the Grade of the Tumor

Stage of Tumor	Age Groups					
	21 – 30 Years		31 – 40 Years		Total	
	No.	%	No.	%	No.	%
Low grade (G <sub>1</sub> and G <sub>2</sub> )	8	40.0	10	50.0	18	100.0
High grade (G <sub>3</sub> )	0	0	2	10.0	2	10.0
Total	8	40.0	12	60.0	20	100.0

Statistical Analysis 0.49

This data is unable to elicit the significant association between age and stage Association of Age with Recurrence tumor

Recurrence at First Check Cystoscopy (After 3 Month)	Age Groups					
	21 – 30 Years		31 – 40 Years		Total	
	No.	%	No.	%	No.	%
Yes	0	0.0	4	20.0	4	20.0
No	8	40.0	8	40.0	16	80.0
Total	8	40.0	12	60.0	20	100.0

### Discussion

The carcinoma of urinary bladder is 2<sup>nd</sup> most common malignancy of urinary tract after carcinoma of prostate. It is mainly disease of old age<sup>8</sup> and rare in younger age (40 years). In young patients incidence of disease varies like 0.8%,<sup>4</sup> 1%<sup>9</sup> and 3.6%.<sup>5</sup> There are conflicting reports about the prognosis of disease. Benson noted favorable prognosis of disease in younger age group.<sup>10</sup> While Madgar et al<sup>11</sup> and Fitzpatrick<sup>12</sup>

noted that prognosis depends upon grade and stage at the presentation rather than age. The age limit of 40 years has been taken by many researchers because the incidence of transitional cell carcinoma of urinary bladder rises sharply after 40 years.<sup>4</sup>

In our study male to female ratio was 4: 1 indicating the usual male domination in carcinoma of bladder. It is similar to study of Slawomir Poletajew,<sup>4</sup> but in other studies it varied from 3:1.<sup>6</sup> In another study

reported by Johnson Hills<sup>12</sup> it was 7:1. Our results in this regard are closer to international literature.

In our study 40% of patients were between the age of 21 – 30 years and 60% were in range of 31 – 40 years which are similar to study of Kutarski, Padwell<sup>13</sup> and Slawomir Poletajew.<sup>4</sup>

The carcinoma of urinary bladder is known to be more prevalent with certain occupations. In our study farmers and industrial workers were mostly (60%) involved as far as profession is concerned. These results are comparable with the study of Fernandez – Fernandez.<sup>14</sup> The farmer are usually exposed to a large number of carcinogens like fertilizer and pesticides, so as are factory workers being at an increased risk of ingestion and inhalation of different carcinogens especially boiler engineering and metal industry.

Cigarette smoking is clearly the most important single known risk factor of bladder cancer.<sup>15</sup> In our study, 30% patients were smokers. However the percentage of smokers in young patients varies from 46 – 59% as reported by Kurtz et al<sup>16</sup> and Kutarski and Padwell<sup>8</sup> respectively. A small study population in our case may be the reason for relatively low incidence of relationship with smoking.

In our study, all the patients presented with hematuria. While 20% of patients had associated irritative voiding symptoms with hematuria. In younger age group the predominant symptoms of hematuria was noted in 90% to 93% by Yu – chug wen.<sup>17</sup> Fitzpatrick, Reda noted 10% of their patients presented with irritative bladder symptoms.<sup>12</sup>

At initial presentation 90% of patients were having solitary lesion while 10% were having multiple lesion disease. Our results regarding multiple lesions patterns are different from Kutarski and Padwell,<sup>13</sup> in which they noted 26% of patients having multiple lesions at the time of presentation. This difference could be due to small number of patients in our study.

In our study 90% patients had low grade disease and 10% had high grade disease. These results regarding grade are similar as reported by Yu Chung Wen.<sup>17</sup> The low grade of disease is one of the most important contributory factors for the better prognosis of the disease. The low grade disease may well recur but progression is rare as compared to high grade disease.<sup>18,19</sup> The 80% of our patients had superficial disease; while 20% had muscle invasive disease. The reported incidence of muscle invasion at initial presentation is 20% reported by Yu – Chen Wen.<sup>17</sup> So our results are comparable with other studies. While in old age 75% have

superficial disease and 25% have muscle invasive disease at the time of initial diagnosis.<sup>8</sup> The recurrence of disease depends upon the number of growths, size of growth; stage and grade of growth. There were 16 patients who were having superficial disease at initial diagnosis. These 16 patients having superficial disease only one patient in this group 1 has pT<sub>1</sub> G<sub>II</sub> and 3 patients in group II were pT<sub>1</sub> G<sub>II</sub>. All these four patients of stage pT<sub>1</sub> G<sub>II</sub> were subjected to intravesical BCG therapy. Only 2 (12.5%) patients in group II had recurrence at first check cystoscopy after 3 month. Their growth was resected completely and they had same stage and grade. In the study of Yu-Ching Wen et al<sup>17</sup> a progression of 8.3% was observed. This difference may because of their longer follow up. Kutarski and Padewell<sup>13</sup> noted the recurrence rate of 42% in younger age patients. The reason for this higher recurrence rate was that in their study 26% patients had multiple lesions, while in our study only 10% patients were having multi – lesion disease. Multi – lesions disease has more potential of recurrence. This recurrence was noted between 31 – 40 years of age. Higher recurrence rate of 45.8% in this age group was noted by Yu-Ching Wen. However no recurrence up to 30 years of age was recorded, as at initial presentation their disease was in low grade and stage. According to Kurtz et al<sup>16</sup> the pathological staging at initial diagnosis was more important than age. We have noted similar situation in our study. The patients in whom recurrence was noted had multiple lesions and moderately differentiated (G<sub>II</sub>) disease at presentation. Among these two patients one was metal factory worker and other was farmer. Madger et al<sup>11</sup> had noted recurrence of disease up to 30 years of age group even with low stage and grade disease.

Among the remaining 4 patients who were having invasive disease at initial presentation two did not turn up on follow up while the other two opted for radiotherapy. A very small size recurrence was noted which was resected in these patients on subsequent check cystoscopy.

## Conclusion

Biological behavior of urothelial bladder cancer depends upon stage and grade. The young patients have good prognosis as they are having low grade and stage.

## References

1. Rubben H, Lutzeyer W, Wallace Dma. The epidemiology and aetiology of bladder cancer. In: Zingg EJ, Wallac DMA (eds). Bladder cancer. New York: Springer – Verlag, 1985: 1-5.
2. Keetch DW, Mainley CB, Catalona WJ. Transitional cell carcinoma of bladder in children and adolescents. *Urology* 1993; 42: 447-49.
3. Gupta NP, Dorairajan LN. Transurethral resection of bladder tumour in pregnancy: A report of 2 cases. *Int Urogynecol J Pelvic Floor Dysfunct* 1997; 8: 230-32.
4. Poletajew S, Waledziak M, Fus M, Pomada P, Ciechanska J, et al. Urothelial bladder carcinoma in young patients is characterized by a relatively good prognosis. *Upsala Journal of Medical Sciences* 2012: 1-5.
5. Stokes MA, Kelly DG. Transitional cell carcinoma in patients under 40 years of age. *Br J Urol* 1986; 59: 536-39.
6. MNM Van Der AA, TH Van Der Kwast, J Prins, R Damhuis, C Bangma, P. Mongiat Artus. Management of non-muscle urothelial tumours: Surgical techniques and pathology.
7. Babjuk M, Oosterlinck W, Sylvester R, Kaasinen E, Bohle A, Palou J, Roupert. Guidelines on non-muscle – Invasive bladder cancer (TaT<sub>1</sub> and CIS). European Association of urology 2012.
8. Badrinath RK and Peter RC. Urothelial carcinoma: cancers of the bladder, ureter and renal Pelvis. *Smith's General Urology*. 17<sup>th</sup> Ed. pp: 308-27.
9. Johnson DE, Hillis S. Carcinoma of bladder in patients less than 40 years old. *J Urol* 1978; 120: 172-73.
10. Benson RC, Tomera Km, Kelalis PP. Transitional cell carcinoma of bladder in children and adolescents. *J Urol* 1983; 130: 54-55.
11. Madgar I, Goldwasser B, Nativ O, Hanani Y, Jonas P. Long term follow-up of patients less than 30 years old with transitional cell carcinoma of bladder. *J Urol* 1988; 139: 933-34.
12. Fitzpatrick Jm, Reda M. Bladder carcinoma in patients 40 years old or less. *J Urol* 1986; 135: 53-54.
13. Kutarski W, Padwell. A transitional cell carcinoma of the bladder in young adults. *Br J Urol* 1993; 72: 749-55.
14. Fernandez – Fernandez A, Gil – Fabra J, Vazquez – Madrano A, Otero – Mauricio G. Occupation and bladder tumour. Results of a study of incident cases. *Actas Urol Esp* 1995; 19 (2): 128-30.
15. Cohen Sm, Johansson SL. Epidemiology and etiology of bladder cancer. *Urol Clin N Am* 1992: 421-28.
16. Kurz KR, Pitts WR, Vaughan ED Jr. The natural history of patients less than 40 years old with bladder tumours. *J Urol* 1987; 137: 395-97.
17. Yu – Ching Wen, Junne – Yih Kuo, Kuang – kuo Chen, Alex TL Lin, Yen – Hwa Changm Yen – Shen Hsu, Luke S. Chang. Urothelial carcinoma of the urinary bladder in young adults-clinical experience at Taipei veterans General hospital. *J chin Med Assoc* 2005; 68 (6): 272-75.
18. Migaldi M, Rossi G, Maiorana A, Sartori G, Ferrari P, De Gaetani C, et al. Superficial papillary urothelial carcinomas in young and elderly patients: a comparative study. *BJU Int*. 2004; 94: 311-16.
19. Cho KS, Hwang TK, Kim BW, Yoon DK, Chang SG, Kim SJ, et al. Differences in tumour characteristics and prognosis in newly diagnosed Ta, T<sub>1</sub> urothelial carcinoma of bladder according to patient age. *Urology* 2009; 73: 828-32; 832 el.